

Comparison of Estrogen and Progesterone Receptor Status in Tumor Mass and Axillary Lymph Node Metastasis in Patients with Carcinoma Breast

Abstract

Introduction: Breast malignancy is a hormone-dependent tumor. The hormone receptor status in the primary tumor is required while taking decision for starting adjuvant therapy. The estrogen receptor (ER) and progesterone receptor (PR) status is also an important prognostic marker. **Materials and Methods:** All modified radical mastectomy cases with axillary lymph node dissection were taken. H and E staining was done. All lymph node-positive breast cancer cases were subjected to immunohistochemistry using ER and PR antibodies. **Results:** In the study of 60 cases, the level of concordance between the primary tumor and the metastatic lymph node was 98.33% for ER and 96.66% for PR. **Conclusion:** There exists a positive correlation between the hormone receptor status of the primary tumor and the paired axillary lymph nodes.

Keywords: Carcinoma breast, estrogen receptor, progesterone receptor

Introduction

In spite of an outstanding research in the field of treatment of breast malignancy over the past decades, the condition still remains being a major challenge overall. Breast carcinoma can be defined as an uninhibited proliferation of the cells of the mammary gland epithelium. This illness can affect both the sexes. The second most malignancy overall is the malignancy of the breast.

The incidence keeps rising with the age. Breast malignancy constitutes 29% of all new cancer cases and also 14% of all cancer-associated mortality among females worldwide up to the year 2012.^[1] According to GLOBOCAN 2012, the worldwide incidence is 1,670,848 and the 5-year prevalence is 239.9/lakh. In India, the incidence is 144,903 and the 5-year prevalence is 92.6/lakh.^[2]

Conventionally, hormone receptor status is assessed only for the primary tumor. Recently, attempts have been taken to evaluate the receptor status in the metastatic lymph node as well. If receptor expression levels in the metastatic disease differ from the primary tumor, this might be an important reason for treatment failure.

Cancer is a complex disease which displays considerable heterogeneity at tumor and molecular level, and a comprehensive analysis of differences in receptor expression between primary and nodal diseases is required.^[3]

Aim and objectives

The aim of this study was to establish a correlation between estrogen receptor (ER) and progesterone receptor (PR) status in positive lymph nodes akin to the ER and PR status in tumor mass of carcinoma breast patients.

Objectives

1. To confirm the diagnosis of breast malignancy and lymph node positivity status on histopathology
2. To assess and evaluate for hormone receptors (ER and PR) status in tumor mass and lymph nodes which are positive for metastasis
3. To compare expressions of ER and PR between primary tumor and axillary lymph node metastasis.

Materials and Methods

The present study is an observational analytical cross-sectional study. It was conducted in

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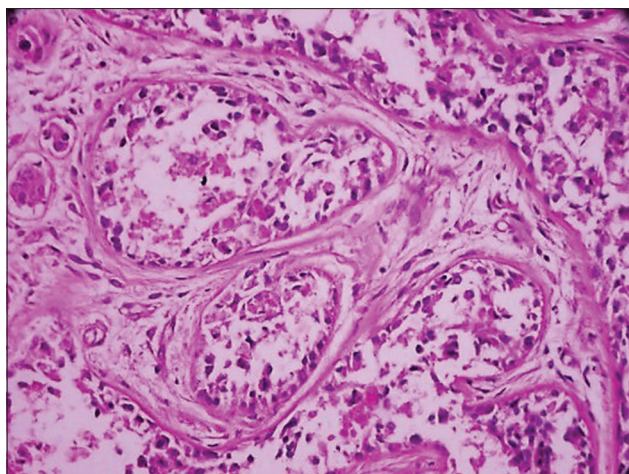


Figure 1: H and E-stained section from tumor mass of breast shows histopathological features of infiltrating duct carcinoma (not otherwise specified type) Grade 1 (x40 view)

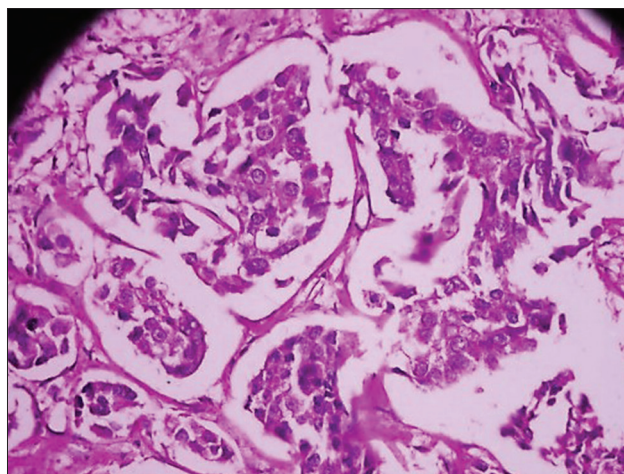


Figure 2: H and E-stained section from tumor mass of breast shows histopathological features of IDC (NOS type) Grade 2 (x40 view)

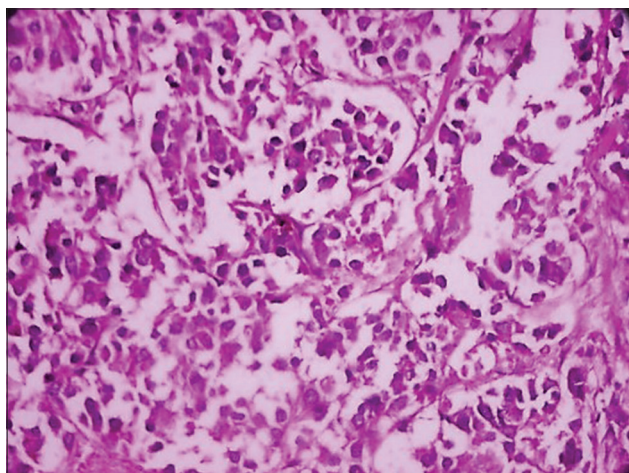


Figure 3: H and E-stained section from tumor mass of breast shows histopathological features of IDC (NOS type) Grade 3 (x40 view)

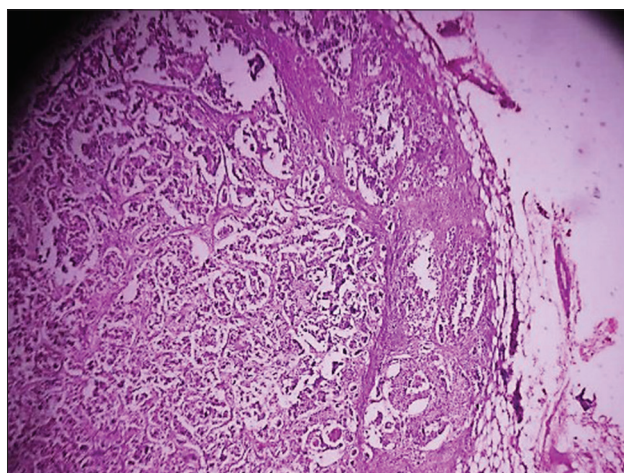


Figure 4: H and E-stained section from axillary lymph node shows histopathological features of infiltrative deposits of malignant ductal epithelial cells suggesting metastatic lymph node (x10 view)

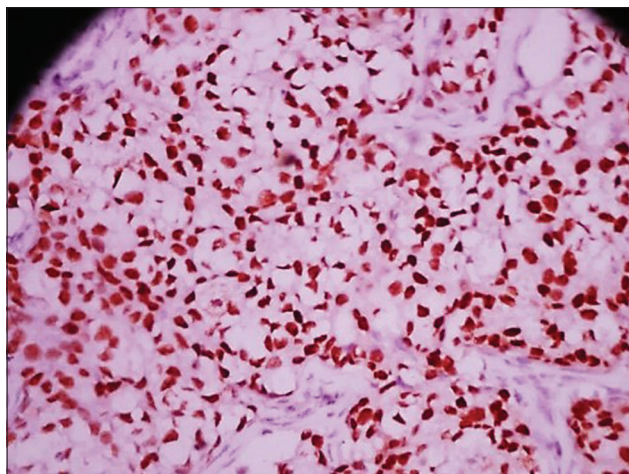


Figure 5: Section stained with immunohistochemical stain (estrogen receptor) shows nuclear positivity in tumor mass (x40 view)

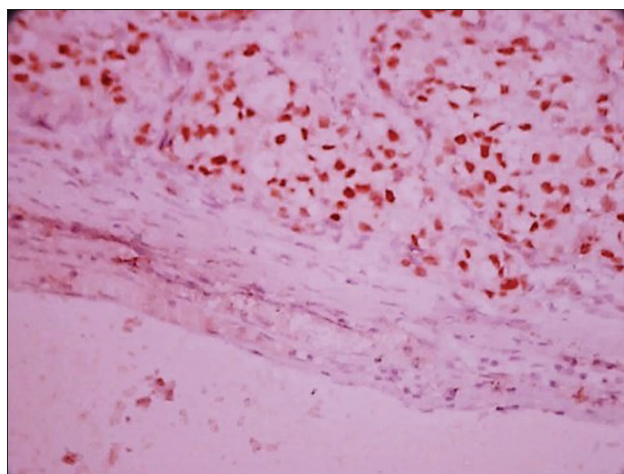


Figure 6: Section stained with immunohistochemical stain (progesterone receptor) shows nuclear positivity in tumor mass (x40 view)

the histopathology and immunohistochemistry (IHC) section of the Department of Pathology, Jawaharlal Nehru Medical

College and AVBRH, Sawangi (Meghe), Wardha, from August 1, 2016, to July 31, 2018.

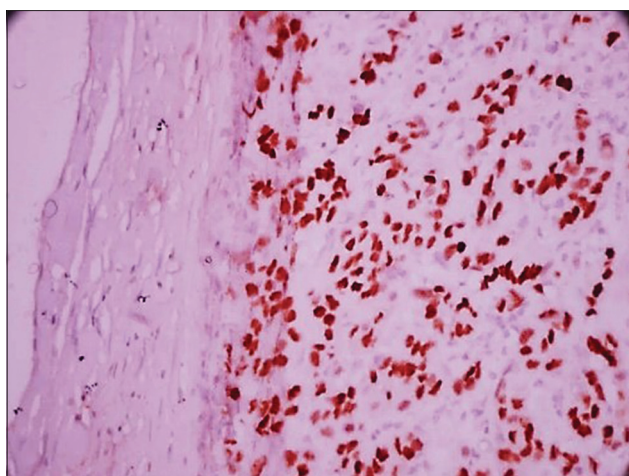


Figure 7: Section stained with immunohistochemical stain (estrogen receptor) shows nuclear positivity in metastatic node ($\times 40$ view)

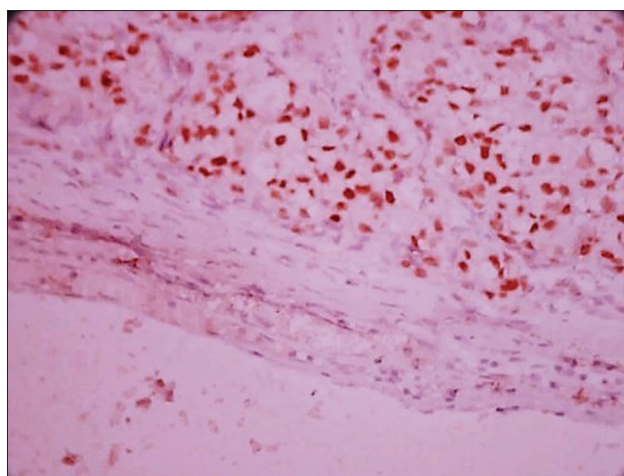
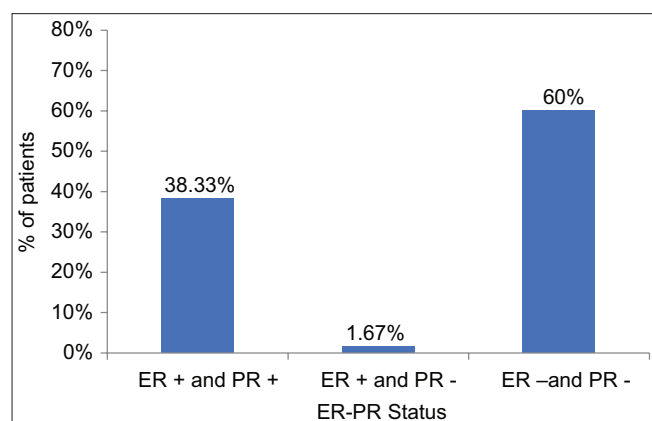


Figure 8: Section stained with immunohistochemical stain (progesterone receptor) shows nuclear positivity in metastatic node ($\times 40$ view)



Graph 1: Distribution of cases based on estrogen receptor and progesterone receptor status of tumor mass

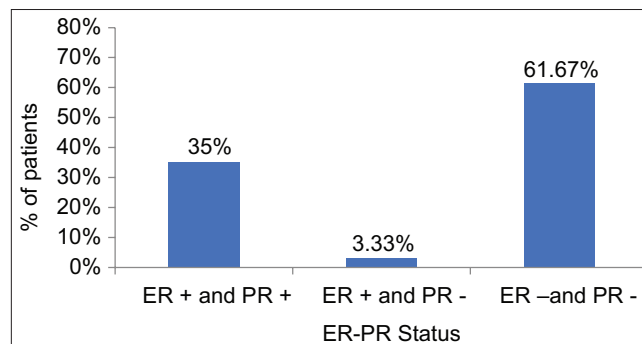
The study was undertaken with the approval of the Institutional Ethics Committee. Informed consent was taken from all the patients who were included in the study. H and E staining was done on modified radical mastectomy (MRM) specimens [Figures 1-3], and lymph node-positive cases [Figure 4] were taken. All these cases were further subjected to IHC for ER-PR status both in the tumor mass and the metastatic lymph node [Figures 5-8]. Later, the ER-PR status was compared between the lymph node and the tumor mass.

Inclusion criteria

Female patients diagnosed with invasive ductal carcinoma of the breast on fine-needle aspiration, patients who underwent MRM, and patients who were diagnosed with invasive ductal carcinoma and positive metastasis on deposits were included in the study.

Exclusion criteria

Cases where only Tru-Cut biopsy or lumpectomy or quadrantectomy has been done, as in such cases, all the parameters will not be available for assessment and cases



Graph 2: Distribution of cases based on estrogen receptor and progesterone receptor status in lymph node

Table 1: Allred scoring system

PS	Observation (%)	IS	Observation
0	None	0	None
1	1	1	Weak
2	1-10	2	Intermediate
3	10-33	3	Strong
4	33-66		
5	66-100		

Sum of PS and IS

Final score	Interpretation
0-2	Negative
3-8	Positive

PS: Proportion score; IS: Intensity score

Table 2: Distribution of cases based on estrogen receptor and progesterone receptor status in tumor mass

ER-PR status	Number of patients (%)
ER+ and PR+	23 (38.33)
ER+ and PR-	1 (1.67)
ER- and PR-	36 (60)
Total	60 (100)

ER: Estrogen receptor; PR: Progesterone receptor

where neoadjuvant chemotherapy is already taken by the patients, were excluded from the study.

Materials for immunohistochemical staining estrogen receptor and progesterone receptor

Dako-pharmDX™ IHC kit includes monoclonal mouse anti-human ER antibody, monoclonal mouse anti-human PR antibody, and epitope retrieval solution. Avidin biotin complex method was used.^[4] External positive controls for ER and PR: Cases of invasive breast carcinoma were taken as positive controls. On immunohistochemical staining, ER and PR show brownish-colored nuclear positivity in the mammary glands. The scoring for IHC is done using Allred score [Table 1].^[4]

Results

Sixty cases which were diagnosed as infiltrating ductal carcinoma with axillary lymph node metastasis on histopathology constituted the study group. For convenience, cases were classified as ER+PR+, ER+PR-, and ER-PR-.

The hormone status was conducted in tumor mass. Of sixty cases, 23 (38.33%) cases were ER+PR+, 1 (1.67%) case was ER+PR-, and ER-PR- status was seen in 36 (60%) cases. Hence, most of the cases belonged to the ER-PR- category [Table 2 and Graph 1].

When hormone receptor status was conducted in the metastatic lymph nodes, it was found that of 60 cases, 21 (35%) cases were ER+PR+, 2 (3.33%) cases were ER+PR-, and 37 (61.67%) cases were ER-PR-. Hence, most of the cases belonged to the ER-PR- category [Table 3 and Graph 2].

Finally, the ER-PR status of tumor mass and lymph node was compared. Of 60 cases, 35% of the cases were positive for both ER and PR in both lymph node and tumor mass. On the other hand, 60% of the cases showed a similar status of receptor negativity in both the tumor mass and lymph nodes.

Table 3: Distribution of cases based on estrogen receptor and progesterone receptor status in lymph node

ER-PR status	Number of patients (%)
ER+ and PR+	21 (35)
ER+ and PR-	2 (3.33)
ER- and PR-	37 (61.67)
Total	60 (100)

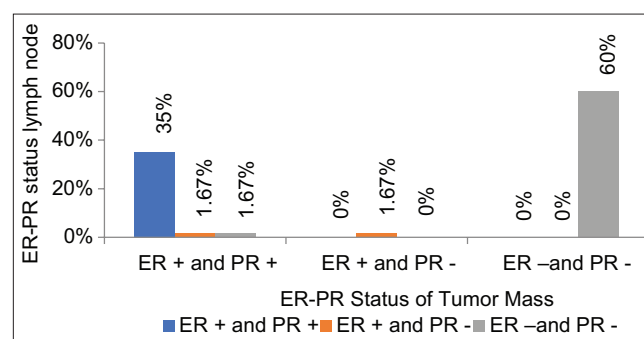
ER: Estrogen receptor; PR: Progesterone receptor

Hence, the concordance level between the tumor mass and the lymph node was 98.33% for ER and 96.66% for PR. When statistical analysis was done using the Chi-square test, it was found that the *P* value was equal to 0.0001 which was significant statistically [Table 4 and Graph 3].

Discussion

Breast malignancy is a hormone-dependent tumor. Endocrine therapy is very helpful in those tumors which do express the ER and PR. It is mandatory to go for the receptor study before starting adjuvant therapy nowadays. Similarly, metastatic lymph node disease is an equally powerful prognostic marker in cases of carcinoma breast. Lymph node metastasis has a role in recurrence and mortality in breast carcinoma patients. Since the chances of survival after recurrence is very less in node-positive patients than in participants with node-negative ones, there is always a probability that nodal metastatic disease could possibly be having a more aggressive phenotype as compared to the primary tumor.

In the present study, when the ER-PR status of tumor mass and lymph node was compared. Of 60 cases, 35% of the cases were positive for ER and PR in both lymph node and tumor mass. On the other hand, 60% of the cases showed a similar status of receptor negativity in both the tumor mass and lymph nodes. Hence, the concordance level between the tumor mass and the lymph node was 98.33% for ER and 96.66% for PR. When statistical analysis was done using the Chi-square test, it was found that the *P* value was equal to 0.0001 which was significant statistically.



Graph 3: Correlation between estrogen receptor and progesterone receptor status of metastatic lymph node with estrogen receptor and progesterone receptor status F primary tumor

Table 4: Correlation between estrogen receptor and progesterone receptor status of metastatic lymph node with estrogen receptor and progesterone receptor status of primary tumor

Tumor mass	Lymph node (%)			χ^2, P
	ER+ and PR+	ER+ and PR-	ER- and PR-	
ER+ and PR+	21 (35)	1 (1.67)	1 (1.67)	84.53, 0.0001 (significant)
ER+ and PR-	0 (0)	1 (1.67)	0 (0)	
ER- and PR-	0 (0)	0 (0)	36 (60)	
Total	21 (35)	2 (3.33)	37 (61.67)	

ER: Estrogen receptor; PR: Progesterone receptor

In Azam *et al.*'s study,^[5] hundred patients of breast cancer with lymph node involvement were included. On comparing the expression of hormone receptor between the tumor mass and the lymph node, the level of concordance for ER was 91% and for PR was 88%.

Falck *et al.*^[6] conducted their study on 425 patients, of which 297 were lymph node-positive cancers. The degree of concordance of in primary tumor and synchronous positive nodes was 93% for ER, 84% for PR.

In a study by Zhao *et al.*,^[7] fifty-four cases of breast cancer were taken. The kappa value of consistency in the primary tumor and the metastatic lymph nodes was 0.465 for ER, 0.706 for HER2, and 0.445 for PR. No significant discrepancy existed between the two.

In a study by Li *et al.*^[8] on 107 cases of ductal carcinoma, the level of consistency between primary tumor and metastatic lymph node for ER was 77.6% and for PR was 82.2% respectively.

In a study done by Desouki *et al.*,^[9] the level of concordance between the tumor mass and the lymph node was 86.11% for ER and 75% for PR.

The findings in the studies conducted by Azam *et al.*, Falk *et al.*, Zhao *et al.*, and Li *et al.* were consistent with the finding of the present study. The reason behind this is that the malignant cells in the primary tumor which gets metastasized to the axillary group of lymph nodes are the same. Therefore, both the tumor and node have a concordant expression of ER and PR.

In the study conducted by Pakdel *et al.*,^[10] the discrepancy between IHC of primary tumor and synchronous lymph node for ER, PR, and HER2 was 32% ($P = 0.000$), 24% ($P = 0.002$), and 48%, respectively. The reason behind receptor discordance between the tumor and the lymph node could be due to heterogeneity of breast cancer, differences in the timing of fixation and antigen retrieval, and also interobserver variability.

Conclusion

The present study showed that there exists a positive correlation between the hormone receptor status of the primary tumor and the paired axillary lymph nodes. The expression of hormone receptors can be carried out in

the metastatic lymph nodes in cases where primary tumor cannot be assessed. The ER-PR status in the metastatic node will be very helpful while starting the endocrine therapy in patients of carcinoma breast.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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